REMARKS

Claims 2 and 13 are the only claims remaining in the case. All other claims are cancelled. Claims 2 and 13 have hereby been amended to address the issues raised by the examiner and to simplify prosecution of this case. No new issues are presented and claims 2 and 13 are now in *prima facie* condition for allowance.

Specification

Reference to Priority:

Applicant has hereby requested deletion of the sections of the application related to the claim of priority, and the statement of government sponsored research, and replacement of those sections with replacement sections which have been rewritten to include the requisite information in a clear and correct format. Applicant submits that no new matter has been iintroduced by this amendment, and respectfully requests entry of the amendment.

Abstract:

The abstract of the application has been objected to because the first "sentence" is not complete. The previous amendment failed to provide the amended abstract on a separate sheet.

Applicant has hereby amended the abstract to contain a complete first sentence, and the present amendment provides the amended abstract on a separate sheet and marked so as to show the changes.

In view of the foregoing, Applicant respectfully requests withdrawal of this objection.

The abstract has further been amended to include the phrase "or chemical groups" after "individual atoms" in line 14 in order to more accurately reflect the actual procedure that is carried out during optimal ligand design. As described in the specification on page 16 at lines18-22, lead ligand modification is carried out by replacement, deletion or addition of "chemical groups", examples of which are given. Therefore, Applicant submits that this amendment does not introduce new matter and serves to more accurately reflect the invention. Applicant requests entry of this amendment.

35 U.S.C. § 112 Rejection

Claims 2 and 13 stand rejected under 35 U.S.C. § 112 as not enabled. Examiner states that the recitation of calculating a Gibbs free energy of binding of the atom to "an ideal ligand for the atom" is not enabled since the binding of an ideal ligand typically involves the determination of Gibbs free energy fo binding to a group of atoms, and that an ideal ligand would not be "for an atom" but rather for a group of atoms. As Examiner has pointed out, an ideal ligand is defined in the specification on page 11, and further explained on page 10.

Applicant has hereby amended claims 2 and 13 and eliminated the phrase "for the atom" in order to more clearly identify the procedure that is used in the invention. Support for this amendment is found in the specification on page 17 at lie 5-7, where it is stated that the affinity of the ideal ligand is calculated by computing the expected "Gibbs energy of each atom in the protein for an ideal ligand". An ideal ligand is bound to the molecule and contribution to the total Gibbs free energy of binding of the ideal ligand is determined for each atom in the molecule.

In view of the foregoing, Applicant respectfully requests withdrawal of this rejection.

35 U.S.C. § 102(b) Rejection

Claims 2, 6, 8, and 13 stand rejected as being anticipated by Delisi et al., US 5, 495,423. Examiner states that Delisi et al. teaches a computer assisted method and program for predicting the binding affinity of a ligand to a selected binding site in which the coordinates and identity of atoms from a receptor molecule are input into a computer, as is information for atoms of a selected ligand (amino acid or acids), a model of the two is generated, energy of the complex (a 3D model) is minimized, and a binding affinity of the compound for its binding site predicted from the energy minimized structure.

Claims 6 and 8 have hereby been cancelled, therefore making moot this portion of the rejection.

Claims With respect to claims 2 and 13, Applicant has hereby amended claims 2 and 13 to recite the steps of determining the binding site for which the binding affinity of the ligand in question will be calculated. Applicant submits that those steps are novel, as indicated by the allowance of a method containing those steps in issued U.S. patent 6,226,603. Thus the expanded method of the present invention which contains those steps and additionally recites determination of the binding

affinity for the ligand and binding target are also novel.

In view of the foregoing, Applicant respectfully requests withdrawal of this rejection.

35 U.S.C. § 103(a) Rejection

Claims 2, 6-10 and 13 stand rejected under 35 U.S.C. § 103(a) as unpatentable over the combination of DeLisi et al. and Shakhnovich et al. The method of DeLisi et al. is discussed in detail above. Shakhnovich et al. describe a method for structure-based drug design, including the calculation of the free energy of binding. The method is described in detail in column 10 beginning at line 5. In the method, a single hydrogen molecule, H_2, is positioned randomly in the binding site of interest. One of the H atoms is randomly selected to by the site of a new bond. A fragment is then randomly selected from a library of fragments and is attached to the randomly selected H atom. The resulting new fragment is oriented to a position of lowest energy, a second H atom is selected as a site for the attachment of yet another fragment, and so on. In this manner, a molecule which binds to the site with favorable binding energy is constructed piecemeal.

Claims 6-10 have hereby been cancelled, therefore making moot this portion of the rejection.

With respect to claims 2 and 13 of the present application , they have hereby been amended in a manner that distinguishes them from DeLisi et al. , as discussed above. Thus, a combination of DeLisi et al. and Shakhnovich et al. does not render obvious the present invention as claimed since Shakhnovich et al., as stated by Examiner, merely adds the suggestion of adding to a growing energy minimized structure.

In view of the foregoing, Applicant respectfully requests withdrawal of this rejection.

Closing Remarks

In view of the above, claims 2 and 13 should be deemed new and unobvious over the prior art of record. Reconsideration and allowance of the claims at an early date is requested.

Respectfully submitted,

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